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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BRUSCA, JOHN S	
ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/844,662	RASCHKE ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57,63,64,66,68-71 and 87-102* is/are pending in the application.

4a) Of the above claim(s) *91-102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57,63,64,66,68-71 and 87-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. It is brought to the Applicant's attention that a product by process claim is examined for the claimed product only, and that no consideration is given to the method of making the claimed product. See M.P.E.P. 2113. The instant claims are drawn to chromatin that comprises an exogenous protein, however the breadth of the claimed subject matter includes products that have the same structure as naturally occurring protein-chromatin complexes. Claim 68 is drawn to a cell comprising an exogenous polypeptide encoded by a nucleic acid introduced into the cell. however the breadth of the claimed subject matter includes cells that comprise polypeptides encoded by endogenous nucleic acids. The limitation "exogenous" is interpreted as a product by process limitation that includes naturally occurring cellular polypeptides. The limitation also includes naturally occurring complexes that are isolated from a cell.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 57, 63, 64, 66, 68-71, and 87-90 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

It is brought to the Applicant's attention that a product by process claim is examined for the claimed product only, and that no consideration is given to the method of making the claimed product. See M.P.E.P. 2113. The instant claims are drawn to chromatin that comprises an exogenous molecule, however the breadth of the claimed subject matter includes products that have the same structure as naturally occurring protein-chromatin complexes. Claim 68 is drawn to a cell comprising an exogenous molecule encoded by a nucleic acid introduced into the cell.

however the breadth of the claimed subject matter includes cells that comprise polypeptides encoded by endogenous nucleic acids.

Claims 57, 63, 64, 66, 68-71, and 87-90, as written, do not sufficiently distinguish over chromatin complexes with protein as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" See MPEP 2105.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 57, 63, 64, and 87-90 are rejected under 35 U.S.C. 102(b) as being anticipated by Boyes et al. in light of Morceau et al. and Hays and Gregory.

The claims are drawn to a complex of an exogenous molecule bound to chromatin. The binding site is sensitive to a probe of chromatin structure. In some embodiments the exogenous molecule is a zinc finger transcription factor and the probe is DNase I, a chemical probe, or a restriction endonuclease.

Boyes et al. shows in the abstract and throughout reconstitution of chromatin comprising a GATA-1 binding site. Boyes et al. shows that binding of GATA-1 fragments to the

reconstituted chromatin results in disruption of the chromatin structure, as assayed by micrococcal nuclease in figures 1 and 4, and DNase 1 in figure 4. Boyes et al. shows that binding of full length GATA-1 to the reconstituted chromatin results in disruption of the chromatin structure, as assayed by DNase 1 in figure 6.

Morceau et al. reviews the properties of GATA-1, and shows that it is a zinc finger protein on page 537, 542-543, and figure 1.

Hayes reviews the use of chemical probes to analyze chromatin structure. Hayes lists in Table 1, page 130 numerous chemical probes that can be used to assay chromatin structure. Hayes serves to show that chromatin structure can be probed by chemical probes.

Gregory reviews the general applicability of restriction endonucleases as probes to analyze chromatin structure. Gregory serves to shows that chromatin structure can be probed by restriction endonucleases.

5. Claims 57, 63, 64, 66, 68, 70, 71, and 87-90 are rejected under 35 U.S.C. 102(b) as being anticipated by Stamatoyannopoulos et al. in light of Morceau et al. and Hays and Gregory.

The claims are drawn to a complex of an exogenous polypeptide bound to chromatin. The binding site is sensitive to a probe of chromatin structure. In some embodiments the exogenous polypeptide is a zinc finger transcription factor and the probe is DNase I, a chemical probe, or a restriction endonuclease. In some embodiments a cell comprises the complex, and the cell is a human cell.

Stamatoyannopoulos et al. shows in the abstract and throughout analysis of a GATA-1 binding site in the human beta globin locus control region (LCR). Stamatoyannopoulos et al. shows analysis of two types of cells, mouse erythroleukemia cells (MEL) stably transformed

with constructs of the LCR in which the GATA-1 binding site in the LCR is either mutated or normal by use of DNase 1 in figures 2-5, and additionally Namalwa human lymphoid cells comprising a human LCR region using micrococcal nuclease in figure 6. Stamatoyannopoulos et al. shows that the LCR region chromatin structure can be analyzed by DNase 1. Stamatoyannopoulos et al. concludes from comparison of mutated and normal GATA-1 binding sites in the LCR that binding of GATA-1 results in disruption of chromatin structure in the LCR.

Morceau et al. reviews the properties of GATA-1, and shows that it is a zinc finger protein on page 537, 542-543, and figure 1.

Hayes reviews the use of chemical probes to analyze chromatin structure. Hayes lists in Table 1, page 130 numerous chemical probes that can be used to assay chromatin structure. Hayes serves to show that chromatin structure can be probed by chemical probes.

Gregory reviews the general applicability of restriction endonucleases as probes to analyze chromatin structure. Gregory serves to shows that chromatin structure can be probed by restriction endonucleases.

6. Claims 57, 63, 66, 70, 87, 88, 89, and 90 are rejected under 35 U.S.C. 102(b) as being anticipated by Truss et al. in light of Beato et al.

The claims are drawn to a complex of an exogenous molecule bound to chromatin. The binding site is sensitive to a probe of chromatin structure. In some embodiments the probe is DNase I, a chemical probe, or a restriction endonuclease. In some embodiments the claims are drawn to an animal cell comprising the complex.

Truss et al. shows analysis of chromatin structure in a mouse mammary tumor virus integrated promoter in mouse cells. Truss et al. shows that addition of exogenous dexamethasone

or R5020 steroid hormone to cells results in rearrangement of the chromatin structure in the abstract and figures 2, 5 (analyzed by chemical digestion), figures 3, 4, 6, 7, 9 (analyzed by DNase I and micrococcal nuclease digestion), and figure 8 (analyzed by restriction endonuclease digestion). Truss et al. shows the hormone receptor binds to the chromatin site on page 1747, and that the addition of hormone induces chromatin rearrangement on pages 1748-1749. Truss et al. does not make clear that a complex of steroid and hormone receptor binds to chromatin.

Beato et al. reviews transcriptional regulation by steroid hormone receptors, and shows in the abstract and page 241 that steroid hormone receptors bind steroid hormones which cause a conformational change in the steroid hormone receptor. The steroid-receptor complex then binds to chromatin to effect gene expression.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 57, 87, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyes et al. in view of Hays in view of Gregory.

The claims are drawn to a complex of an exogenous polypeptide bound to cellular chromatin. In some embodiments the binding site is sensitive to a chemical or restriction endonuclease probe of chromatin structure.

Boyes et al. shows in the abstract and throughout reconstitution of chromatin comprising a GATA-1 binding site. Boyes et al. shows that binding of GATA-1 fragments to the reconstituted chromatin results in disruption of the chromatin structure, as assayed by micrococcal nuclease in figures 1 and 4, and DNase 1 in figure 4. Boyes et al. shows that binding of full length GATA-1 to the reconstituted chromatin results in disruption of the chromatin structure, as assayed by DNase 1 in figure 6. Boyes et al. does not show use of chemical or restriction endonuclease probes to analyze chromatin structure.

Hayes reviews the use of chemical probes to analyze chromatin structure. Hayes lists in Table 1, page 130 numerous chemical probes that can be used to assay chromatin structure. Hayes serves to show that chromatin structure can be probed by chemical probes.

Gregory reviews the general applicability of restriction endonucleases as probes to analyze chromatin structure. Gregory serves to shows that chromatin structure can be probed by restriction endonucleases.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the chromatin structure of the complex of Boyes et al. by use of chemical or restriction endonuclease probes of chromatin structure because Hayes and Gregory show that chemical and restriction endonuclease probes are effective means to analyze chromatin

structure. Performing such analysis would establish that the chromatin-GATA-1 complexes of Boyes et al. are species of the claimed subject matter of claims 57, 87, and 90.

10. Claims 57, 87, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamatoyannopoulos et al. in view of Hays in view of Gregory.

The claims are drawn to a complex of an exogenous polypeptide bound to chromatin. The binding site is sensitive to a probe of chromatin structure. In some embodiments the binding site is sensitive to a chemical or restriction endonuclease probe of chromatin structure.

Stamatoyannopoulos et al. shows in the abstract and throughout analysis of a GATA-1 binding site in the human beta globin locus control region (LCR). Stamatoyannopoulos et al. shows analysis of two types of cells, mouse erythroleukemia cells (MEL) stably transformed with constructs of the LCR in which the GATA-1 binding site in the LCR is either mutated or normal by use of DNase 1 in figures 2-5, and additionally Namalwa human lymphoid cells comprising a human LCR region using micrococcal nuclease in figure 6. Stamatoyannopoulos et al. shows that the LCR region chromatin structure can be analyzed by DNase 1. Stamatoyannopoulos et al. concludes from comparison of mutated and normal GATA-1 binding sites in the LCR that binding of GATA-1 results in disruption of chromatin structure in the LCR. Stamatoyannopoulos et al. does not show use of chemical or restriction endonuclease probes to analyze chromatin structure.

Hayes reviews the use of chemical probes to analyze chromatin structure. Hayes lists in Table 1, page 130 numerous chemical probes that can be used to assay chromatin structure. Hayes serves to show that chromatin structure can be probed by chemical probes.

Gregory reviews the general applicability of restriction endonucleases as probes to analyze chromatin structure. Gregory serves to shows that chromatin structure can be probed by restriction endonucleases.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the chromatin structure of the complex of Stamatoyannopoulos et al. by use of chemical or restriction endonuclease probes of chromatin structure because Hayes and Gregory show that chemical and restriction endonuclease probes are effective means to analyze chromatin structure. Performing such analysis would establish that the chromatin-GATA-1 complexes of Stamatoyannopoulos et al. are species of the claimed subject matter of claims 57, 87, and 90.

11. Claims 57, 66, and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamatoyannopoulos et al. in view of Greisman et al.

The claims are drawn to a complex of an exogenous polypeptide bound to chromatin. The binding site is sensitive to a probe of chromatin structure. In some embodiments the claims are drawn to a plant cell comprising the complex.

Stamatoyannopoulos et al. shows in the abstract and throughout analysis of a GATA-1 binding site in the human beta globin locus control region (LCR). Stamatoyannopoulos et al. shows analysis of two types of cells, mouse erythroleukemia cells (MEL) stably transformed with constructs of the LCR in which the GATA-1 binding site in the LCR is either mutated or normal by use of DNase 1 in figures 2-5, and additionally Namalwa human lymphoid cells comprising a human LCR region using micrococcal nuclease in figure 6. Stamatoyannopoulos et al. shows that the LCR region chromatin structure can be analyzed by DNase 1.

Stamatoyannopoulos et al. concludes from comparison of mutated and normal GATA-1 binding sites in the LCR that binding of GATA-1 results in disruption of chromatin structure in the LCR. Stamatoyannopoulos et al. does not show plant cells comprising exogenous polypeptides bound to chromatin.

Greisman et al. teach a strategy for selecting high-affinity zinc finger proteins for diverse DNA target sites. Greisman et al. shows a strategy for selecting high-affinity zinc finger proteins for diverse DNA target sites. Additionally, at column 7, lines 29-30, they state that the zinc finger proteins provide means for developing plants with altered phenotypes.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the complex of Stamatoyannopoulos et al. by use of a complex of a zinc finger protein with chromatin in a plant cell in view of the conventionality of doing so taught by Greisman et al. for the purpose of pursuing research to develop plants with altered phenotypes.

Response to Arguments

12. Applicant's arguments filed 14 March 2007 have been fully considered but they are not persuasive. The applicants state that the limitation of "exogenous molecule" excludes a naturally occurring complex. However the definition in the specification of exogenous molecule on page 11 pointed to by the applicants does not have a structural limitation that distinguishes the structure of exogenous molecules from that of naturally occurring molecules. Instead, the definition refers to the source and process of introduction of the molecule. The definition states that an exogenous molecule is a molecule that is not normally present in a cell, but is introduced into the cell by one or more genetic, biochemical or other methods, which is a limitation on the

location of the molecule and its process of introduction rather than the structure of the molecule. Any molecule that is isolated is a molecule that is not present in a cell. A molecule isolated from a cell is exogenous to the cell after isolation. The limitation is not a functional limitation as argued by the applicants, but is rather a limitation as to prior location and process of introduction, which could be achieved by a process that includes initial isolation from a cell, or synthesis by chemical or biological methods, of any molecule. The claims read on any product that could be made by a process of introduction of an exogenous molecule. Since it is routine in the art to introduce isolated proteins of choice or to introduce isolated polynucleotides encoding proteins of choice, any cellular protein could be made by a process of introduction to a cell of the protein or a gene encoding the protein. Therefore the product by process limitation of "exogenous" is met by any cellular protein. The claims do not discriminate between complexes comprising molecules with structures different from products of nature and complexes comprising naturally occurring molecules.

It is further noted that the specification states on page 16 that endogenous molecules may be present at the particular developmental stage of the cell. In other words, an exogenous molecule can be a protein that is expressed from the genome of the cell at a different developmental stage. The claimed complex between such a developmentally regulated protein and its target would be a product of nature because it would occur at the appropriate developmental stage.

The applicants state that the claims require the hand of man, but the claims are not limited to isolated complexes or complexes comprising molecules with structures different than products of nature.

Because the claims read on products of nature, the rejection under 35 U.S.C. 101 is maintained.

The applicants reiterate the arguments addressed above in their discussion of the rejections under 35 U.S.C. 102 and 103. The applicants state that the rejections over Boyes et al. under 35 U.S.C. 102 and 103 are invalid because Boyes et al. shows analysis of isolated chromatin, however the specification defines chromatin on page 10 as a nucleoprotein without a limitation as to its location or state of purification. Therefore prior art showing analysis of isolated chromatin meets the claim limitation of cellular chromatin, i.e., chromatin from cells.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

John S. Brusca 29 May 2007

John S. Brusca
Primary Examiner
Art Unit 1631

jsb